Baseline recreational physical activity, history of sports participation, and postmenopausal breast carcinoma risk in the Netherlands Cohort Study.

Baseline Recreational Physical Activity, History of Sports Participation, and Postmenopausal Breast Carcinoma Risk in the Netherlands Cohort Study

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Presented in part at the Annual Scientific Meeting of the Society of Epidemiological Research (SER), Seattle, WA, June 15–17, 2000, and published in Dirx MJM, van den Brandt PA, Voorrips LE, Goldbohm RA. Current and past physical activity and postneuropausal breast cancer risk in the Netherlands Cohort Study [abstract] *Am J Epidemiol* 2000;151(11):S63.

The Netherlands Cohort Study was supported by the Dutch Cancer Society.

The authors thank the participants of this study and would also like to thank the Dutch Cancer Registry and the Dutch National Base of Pathology (PALGA) for providing incidence data and S. van de Crommert, H. Brants, J. Nelissen, C. de Zwart, and W. van Dijk for assistance in the cohort study.

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Received May 2, 2001; accepted June 6, 2001.

BACKGROUND. The aim of the current study was to evaluate the relation between physical activity and breast carcinoma risk with specific emphasis on interaction with other aspects of energy balance.

METHODS. The Netherlands Cohort Study on diet and cancer was conducted among 62,537 women ages 55–69 years at baseline. Information regarding baseline recreational physical activity, history of sports participation, and occupational physical activity was collected with a questionnaire in 1986. After 7.3 years of follow-up, 1208 incident breast carcinoma cases were available for case-cohort analyses.

RESULTS. A summed total of baseline recreational physical activity (including walking, cycling, gardening) showed an inverse association with breast carcinoma risk. Women who were active in the above-mentioned activities for $>$ 90 minutes a day had a rate ratio (RR) of 0.76 (95% confidence interval [95% CI], 0.58–0.99) compared with women who were active $<$ 30 minutes a day. Women who ever participated into sports before baseline had a RR of 1.13 (95% CI, 0.94–1.37) compared with women who never participated in sports. The relation between sports participation and breast carcinoma risk did not appear to be dependent on the time window of participation (before/after menarche, before/after birth of the first child, before/after age 20 years). No interaction was found between baseline recreational physical activity, body mass index (BMI) (kg/m^2), energy intake, and weight gain/loss during adult life in relation to breast carcinoma, although in the subgroup of women with a high BMI we found a stronger inverse relation between recreational physical activity and breast carcinoma risk independent of energy intake. Occupational physical activity was not found to be related to breast carcinoma risk.

CONCLUSIONS. The current study findings support the hypothesis that recreational physical activity is associated inversely with breast carcinoma risk. ***Cancer* 2001;92: 1638–49.** © *2001 American Cancer Society.*

KEYWORDS: physical activity, breast carcinoma, body mass index (BMI), energy intake.

Many studies have examined the role of physical activity in the etiology of breast carcinoma. Decreased breast carcinoma risk associated with regular physical activity first was suggested by Frisch et al.[1] when they reported a significantly greater prevalence of breast carcinoma among women who were not involved with athletics in college compared with athletes 1–56 years after graduation. Since then, to our knowledge more than 20 epidemiologic studies have been published from the U.S., Europe, Australia, and Japan. These studies have investigated the relation between breast carcinoma and

occupational and/or recreational physical activity. The study designs, population samples, measures of physical activity, and outcome varied widely. The populations studied ranged from occupation-based or education-based cohorts to hospital-based case–control studies. Some studies compared women according to participation in college sports, some examined occupational physical activity only, several examined recreational physical activity only, and others studied both occupational and recreational physical activity. Physical activity assessment methods used across studies have been quite heterogeneous. The majority of the studies used questionnaires but the questions asked varied substantially. Often the studies relied on reported hours per week doing exercise, or respondents had to classify themselves as lightly, moderately, or strenuously physically active.[2]

Four cohort studies[1,3–5] reported that recreational exercise reduces the risk of developing breast carcinoma, at least among certain subgroups of women. No association was reported in three other cohort studies[6–8] and an increased risk of breast carcinoma was reported to be associated with higher levels of physical activity in the Framingham cohort study.[9] The majority of the population-based[10–15] and hospital-based case–control[16–18] studies have reported an inverse association with recreational activity. One case–control study found an increased breast carcinoma risk.[19]

The studies concerning occupational physical activity showed inconclusive results. To our knowledge, to date it is unclear whether occupational physical activity protects against breast carcinoma in premenopausal women,[20] postmenopausal women,[21] or women of all ages.[5,16,22]

Several possible biologic mechanisms have been postulated as an explanation for the observed protective effect of physical activity and the risk of breast carcinoma. These have focused on exercise and sex hormone interactions, exercise and immune function, and exercise and energy balance.[23]

There is some evidence to suggest that physical activity can influence at least some of the aspects of menstrual history, and it has been suggested that if physical activity does modify breast carcinoma risk, it might do so through a hormone-related pathway. Strenuous physical exercise before menarche is believed to delay the onset of menstruation and to increase the number of anovulatory cycles, therefore reducing cumulative (lifetime) estrogen exposure. Bernstein et al. reported that moderate physical exercise during adolescence reduces the number of ovulatory cycles and increases menstrual cycle length patterns.[24]

It also has been suggested that exercise may influence breast carcinoma development through concurrent changes in immune function. Despite the evidence that training enhances natural immune function, the biologic relevance for breast carcinoma risk is not known.[23] It also has been postulated that energy balance could have an influence on breast carcinogenesis. Energy balance is defined by a state in which energy intake is equal to energy expenditure, resulting in no net change of energy stores in the body. The aspects of energy balance that have been linked to the etiology of breast carcinoma include low physical activity and an excess accumulation of body weight. The relation between these two risk factors is complex and to our knowledge the mechanism relating them to an increased risk of breast carcinoma is unknown.[23]

To our knowledge, it is yet not known what the magnitude of the effect is; what intensity, duration and frequency of activity are required for a reduction in breast carcinoma risk; and what time period(s) in a woman's life are important in such a risk reduction. Therefore, we conducted the current study to evaluate the relation between physical activity and breast carcinoma risk in postmenopausal women in an ongoing cohort study. Furthermore, we were interested in modification by the different time windows in which women were physically active and studied the possible interaction with other indicators of energy balance with regard to breast carcinoma risk.

MATERIALS AND METHODS

The current study was conducted in an ongoing prospective cohort study on diet and cancer, the Netherlands Cohort Study (NLCS), among 62,573 women ages 55–69 years at baseline. Baseline exposure data were collected by means of a self-administered questionnaire in 1986. The questionnaire referred to dietary habits and potential confounders such as reproductive history, reported height and weight, education, and family history of cancer. Also included were questions regarding baseline recreational physical activity, history of sports participation, and occupational history. A detailed description of the cohort study design has been reported elsewhere.[25] After the baseline exposure measurement, a subcohort was sampled randomly from the cohort and followed biennially for information concerning vital status. Incident cancer cases occurring in the entire cohort have been identified by record linkage to cancer registries and a national pathology register (PALGA). The method of record linkage has been described previously.[26]

The collected data from subcohort and breast carcinoma cases were key-entered twice by research as-

sistants who were blinded with respect to subcohort/case status to minimize observer bias in coding and interpretation of the data. After 7.3 years of follow-up, 1208 breast carcinoma cases were available for analysis, after exclusion of prevalent cancer cases and cases with in situ breast carcinoma. Prevalent cancer cases other than skin cancer also were excluded from the subcohort, after which 1716 women remained. For data analysis the case–cohort approach was used in which cases were derived from the entire cohort, whereas the person-years at risk were estimated from the subcohort.

Baseline Recreational Physical Activity

Assessment of baseline recreational physical activity was based on two questions. The first question was "How many minutes do you spend on average per day walking or cycling to your work, to go shopping, or to take out your dog?" The subjects could fill in the number of minutes spent per day on these activities. The minutes spent per day on these activities were categorized: $<$ 30 minutes a day, 30–60 minutes a day, 60–90 minutes a day, and $>$ 90 minutes a day.

The second question was: "How many hours of your leisure time do you spend on average per week on the following activities: gardening/doing odd jobs, cycling/walking (other than in first question), and sports/gymnastics?" Possible answers were never, $<$ 1 hour, 1–2 hours, or $>$ 2 hours per week. We added the time spent on these activities up to an overall measure (minutes per day). Baseline recreational physical activity was used as the combination of the number of minutes spent per day biking/walking, shopping, and walking the dog and the number of hours spent per week on gardening/doing odd jobs, cycling/walking, and sport/gymnastics. Women who participated in sports at baseline could fill in the type of sport.

History of Sports Participation

Physical activity that took place earlier in time was estimated by asking about the woman's history of sports participation. For each sport, we recorded separately the type of sport, the number of hours per week spent in that sport, and the years in which the participant engaged in that sport. A total of three sports could be mentioned. First, a dichotomization was made in never/ever playing a sport. The total duration of sports activities in years was calculated by summing up the duration of all episodes of playing a sport (accounting for the overlap between sports). The number of total hours per week that the respondent participated in each sport also were added.

We used the compendium of Ainsworth et al.[27] to assign a MET score to each type of sport activity as an indicator of intensity. This method also was used in other studies.[12,13,15,22] A MET score is defined as the ratio of the associated metabolic rate for the specific activity divided by the resting metabolic rate. A total MET score was calculated for the various sports activities, weighted by the duration (in years) of each activity. For example, being active for 10 years in tennis (MET score of 7) and being active for 5 years in recreative swimming (MET score of 8) gave a weighted MET score of $((7 \times 10) + (8 \times 5))/(10 + 5) = 7.3$. For the type of sport at baseline, we assigned a MET score as an indicator of intensity that was not weighted by duration. Sport was defined as an activity with a MET score $>$ 2.5.

Occupational Physical Activity

Subjects were asked for their lifetime occupational history with regard to job title and duration. A total of five jobs could be mentioned. We used information regarding the longest job ever held as well as information concerning the last occupation as indicators of the lifetime physical activity at work. Assessment of physical activity at work was based on job title. Two different measures of occupational physical activity were used: sitting time (hours/day) and energy expenditure (kilojoules [kJ]/minute). The sitting time scale was divided into three groups: low activity ($>$ 6 working hours per day spent sitting), moderate activity (2–6 hours per day spent sitting), and high activity ($<$ 2 working hours per day sitting). The total energy expenditure was based on a rating system developed by Hettinger et al.[28] Low activity included work with an energy expenditure $<$ 8 kJ/minute, moderate activity was defined as an energy expenditure between 8–12 kJ/minute, and high activity corresponded to an activity level $>$ 12 kJ/minute. Housewives were categorized into the moderate group.

Data Analysis

The distribution of the activity variables were compared between breast carcinoma cases and subcohort members. The association between exposure variables and covariates were studied in the subcohort. For the continuous variates age, age at menarche, age at menopause, age at first birth, height, weight at age 20 years, body mass index (BMI) (kg/m^2), alcohol intake and energy intake, mean values of these variables were compared (analysis of variance) between the categories of baseline recreational physical activity, history of sports participation, and occupational physical activity. Covariates associated with breast carcinoma itself or with the exposure variables were considered to be potential confounders. Data were analyzed using the case–cohort approach.[29] Incidence rate ratios (RR)

and corresponding 95% confidence intervals (95% CI) for breast carcinoma were estimated using exponentially distributed failure time regression models[29] with the Stata statistical software package.[30] We conducted several analyses to obtain insight into the periods of life that may be important in the etiology of breast carcinoma. We defined 3 time windows based on the sports participation before and after age 20 years (categories: before/after/before and after age 20 years), sports participation before and after birth of the first child (categories: before/after/before and after birth of the first child), and sports participation before and after menarche (categories: before/after/before and after menarche). Women who never participated in sports were used as the reference category for each subgroup in the analyses.

We conducted several subgroup analyses to assess whether the effect of physical activity on the risk of breast carcinoma was modified by baseline BMI, weight gain/loss during life, baseline energy intake, and modification by the different time windows in which the women were physically active. BMI was categorized according to the standardized categories of the National Institutes of Health (NHI).[31] As a consequence of the small number of cases in the subgroups, we recoded BMI into three categories (BMI of < 25 indicates normal weight, BMI of 25–30 indicates overweight, and BMI of ≥ 30 indicates obese). Energy intake was calculated from the food frequency questionnaire using the computerized Dutch Food Composition Table.[32,33]

RESULTS

Table 1 represents the distribution of the baseline recreational physical activity, history of sports participation, and occupational physical activity (only longest held job is presented) among breast carcinoma cases and subcohort members. The distributions of the variables did not appear differ to a large extent between cases and subcohort members.

The means of potential confounders according to baseline recreational physical activity, history of sports participation, and occupational physical activity among subcohort members is summarized in Table 2. Women who reported being active > 90 minutes per day at baseline were younger, had a later age at menopause, had a lower BMI, and had a higher energy intake at baseline compared with women who were active < 30 minutes per day. Women who had ever engaged in sports activities had a higher energy and alcohol intake at baseline and a lower BMI compared with women who never participated in sports. Women who had a longest held job with a high level of physical activity level (< 2 working hours spent sitting)

TABLE 1
Distribution of the Baseline Recreational Physical Activity, History of Sports Participation, and Occupational Physical Activity in Breast Carcinoma Cases ($n = 1208$) and Subcohort Women ($n = 1716$), The Netherlands Cohort Study (1986–1993)

	Cases[a]		Subcohort[a]	
Exposure variables	**No.**	**%**	**No.**	**%**
Baseline recreational physical activity				
Total recreational physical activity				
< 30 min/day	347	29.2	442	26.3
30–60 min/day	383	32.3	532	31.7
61–90 min/day	226	19.0	355	21.1
> 90 min/day	231	19.5	350	20.9
Daily biking/walking				
< 10 min/day	118	9.9	157	9.3
10–30 min/day	279	23.5	416	24.7
31–60 min/day	405	34.1	539	32.1
> 60 min/day	387	32.5	570	33.9
Gardening/doing odd jobs				
No gardening/doing odd jobs	471	39.6	677	40.3
< 1 h per week	241	20.2	305	18.1
1–2 h per week	229	19.3	334	19.9
> 2 h per week	248	20.9	366	21.7
Sports/gymnastics				
No sports activity	823	69.2	1126	66.9
< 1 h per week	131	11.0	212	12.6
1–2 h per week	163	13.7	247	14.7
> 2 h per week	72	6.1	97	5.8
History of sports participation				
Never	634	53.4	962	57.3
Ever	553	46.6	717	42.7
Duration of sports participation (yrs)				
1–10	271	54.5	346	53.4
11–20	112	22.5	137	21.1
21–30	39	7.9	64	9.9
31–40	26	5.2	47	7.3
> 40	49	9.9	54	8.3
No. of hrs of sports per week				
< 1	111	21.1	146	20.9
1–2	129	24.5	160	22.9
2–3	65	12.4	87	12.4
3–5	75	14.2	121	17.3
> 5	146	27.8	185	26.5
Occupational physical activity				
Longest held job				
Energy expenditure (kJ/min)				
< 8	540	59.2	700	58.3
8–12	328	35.9	426	35.5
> 12	45	4.9	75	6.2
Sitting time per day (hrs)				
6–8	290	31.8	394	32.8
2–6	209	22.9	283	23.5
< 2	414	45.3	525	43.7

kJ: kilojoule.

[a] Due to missing values, the numbers of cases and subcohort women may not add up to 1208 and 1716, respectively.

TABLE 2
Means of Potential Confounders According to Levels of Total Baseline Recreational Physical Activity, History of Sports Participation, and Occupational Physical Activity in the Netherlands Cohort Study, 1986–1993 (subcohort women: n = 1716)

	Baseline recreational physical activity (min/day)				History of sports participation		Occupational physical activity (longest held job) (hrs sitting)		
Characteristics	< 30	30–60	60–90	> 90	No	Yes	6–8	2–6	< 2
Age in 1986 (yrs)	61.9	61.6	61.3	60.9[a]	61.7	61.2	61.0	61.4	61.3
Age at menarche (yrs)	13.6	13.8	13.7	13.7	13.7	13.6	13.5	13.8	13.8
Age at menopause (yrs)	48.2	48.9	48.8	49.1[a]	48.6	49.0	48.6	49.1	48.6
Baseline height (cm)	164.7	165.3	165.3	165.0	164.8	165.4	164.9	165.9	164.9[a]
Baseline weight (kg)	69.2	68.4	68.4	67.8	68.8	68.2	67.1	68.6	68.8[a]
Weight at age 20 yrs (kg)	58.1	58.5	59.3	57.9	58.4	58.5	57.5	58.5	58.8[a]
Weight gain/loss (kg)	11.9	11.0	10.1	10.4[a]	11.2	10.7	10.6	11.0	10.7
Body mass index (kg/m^2)	25.6	25.0	25.0	24.9[a]	25.4	24.9[a]	24.7	24.9	25.3[a]
Energy intake (kcal/day) in 1986	1638	1716	1676	1722[a]	1671	1712[a]	1678	1687	1725
Alcohol (g/day) in 1986	5.0	6.0	6.3	5.8	4.8	6.9[a]	6.8	7.5	4.9[a]
Age at first birth (yrs)	21.7	22.1	22.4	22.4	21.9	22.4	21.6	19.2	22.7[a]

[a] $P < 0.05$ (analysis of variance).

were heavier at baseline and at age 20 years, had a higher BMI, had their first child at a later age, and drank less alcohol compared with women in more sedentary jobs.

Baseline Recreational Physical Activity

Baseline recreational physical activity (daily walking, biking combined with gardening/doing odd jobs, sports) showed an inverse association with breast carcinoma risk. On multivariate analysis, women who were active for > 90 minutes a day had an RR of 0.76, (95% CI, 0.58–0.99; $P = 0.003$) compared with women who were active < 30 minutes a day. The several aspects of baseline recreational physical activity demonstrated the following relations: daily walking/biking showed a significant inverse association with breast carcinoma risk. Women who did these activities for > 1 hour a day had an RR of 0.81, (95% CI, 0.60–1.09; $P = 0.001$) compared with women who did these activities < 10 minutes a day.

Gardening and doing odd jobs were not found to be related to breast carcinoma risk. Baseline sports participation also showed no relation (RR = 0.98; 95% CI, 0.68–1.42) (Table 3). Baseline intensity score for sports showed a small decrease in breast carcinoma risk, although it was not significant. Women who participated in sports with a high intensity (> 6.00 MET score) had an RR of 0.84 (95% CI, 0.55–1.29) compared with women who participated in sports with a low intensity (< 4 MET score) at baseline. Exclusion of cases detected during the first 2 years of follow-up did not change the results.

History of Sports Participation

Women who reported ever to have engaged in a sport had no apparent reduction in breast carcinoma risk compared with women who never participated in a sport. The RR for women who had ever engaged in sports was 1.13 (95% CI, 0.94–1.37) (Table 4) compared with women who never engaged in sports. The total duration of sports in years showed no relation with breast carcinoma. Women who participated in sports > 40 years had an RR of 0.99 (95% CI, 0.58–1.67) compared with women who participated < 10 years. The frequency (hours sport per week) showed a weak inverse relation with breast carcinoma risk. Women who participated 1–2 hours per week, 2–3 hours per week, 3–5 hours per week, and > 5 hours per week into sports had rate ratios of 0.98, 0.88, 0.76, and 0.87, respectively (95% CI, 0.57–1.32; $P = 0.1$), compared with women participating into sports < 1 hour per week (Table 4). The mean intensity score based on history of sports participation and duration in years showed no association with breast carcinoma risk. Women who had a mean intensity score of > 6 METs had an RR of 1.07 (95% CI, 0.71–1.60) compared with women with a mean sport intensity of < 4 METs (Table 4).

Occupational Physical Activity

No relation was found between occupational physical activity and breast carcinoma risk. Women with a high energy expenditure (> 12 kJ/minute) in the longest held job showed a nonsignificantly decreased risk (RR = 0.83; 95% CI, 0.51–1.34) compared with women with a longer held jobs with low energy expenditure (< 8

TABLE 3
Age-Adjusted and Multivariate RRs of Postmenopausal Breast Carcinoma according to Baseline Recreational Physical Activity (Including Sports) and Intensity Scores (MET-Score) Regarding Baseline Sports Activity (the Netherlands Cohort Study, 1986–1993)

	Cases	Person-years	RR[a]	RR[b]	95% CI	*P* value
Baseline recreational physical activity						
Total recreational physical activity (min/day)						
< 30	246	2095	1.00[c]	1.00[c]		
30–60	307	3084	0.90	0.84	0.67–1.07	
61–90	195	2131	0.81	0.78	0.60–1.00	
> 90	193	2113	0.84	0.76	0.58–0.99	0.003
Daily biking/walking (min/day)						
< 10	313	2657	1.00[c]	1.00[c]		
10–30	276	2818	0.92	0.81	0.65–1.02	
31–60	235	2738	0.76	0.71	0.56–0.89	
> 60	117	1211	0.91	0.81	0.60–1.09	0.001
Gardening/doing odd jobs (hrs/week)						
No gardening/odd jobs	367	3520	1.00[c]	1.00[c]		
< 1	186	1814	1.12	1.02	0.80–1.31	
1–2	186	1987	0.98	0.88	0.69–1.13	
> 2	204	2124	0.97	0.93	0.73–1.17	0.23
Sports/gymnastics (hrs/week)						
No sports activity	632	6107	1.00[c]	1.00[c]		
< 1	111	1290	0.85	0.81	0.61–1.06	
1–2	138	1439	0.89	0.90	0.70–1.17	
> 2	62	608	1.00	0.98	0.68–1.42	0.37
MET scores						
Baseline type of sport in 1986						
< 4	66	831	1.00	1.00		
4.01–6.00	82	915	0.75	0.73	0.45–1.17	
> 6.00	158	1514	0.81	0.84	0.55–1.29	0.43

RR: rate ratio; 95% CI: 95% confidence interval; MET score: the ratio of the associated metabolic rate for the specific activity divided by the resting metabolic rate.

[a] Age-adjusted analysis.

[b] Multivariate analysis adjusted for age, age at menarche, age at menopause, benign breast disease, parity, age at first birth, maternal breast carcinoma, breast carcinoma in sister(s), education, height, and baseline alcohol and energy intake.

[c] Reference category.

kJ/min). No relation was found between energy expenditure in last held job and breast carcinoma risk (RR = 0.98). Also, no relation was found between total number of hours spent sitting per day in longest or last held job and breast carcinoma risk (Table 4).

Time Windows

When we examined sports participation in different time windows we found no particular subgroups showing reductions in breast carcinoma risk associated with sports participation. Women who engaged in sports only after the age of 20 years had an RR of 1.03 (95% CI, 0.76–1.40) (Table 5) compared with women who never participated in sports. Women who participated in sports only before, only after, and before and after the birth of their first child had RRs of 1.18, 1.04, and 1.22 (95% CI, 0.89–1.67), respectively, compared with women who never participated in sports. Another subgroup was comprised of women who were physically active only before, only after, and before and after menarche. The subgroup of women who were physically active only before menarche was too small to include in the current analysis. The results showed a slight increase in breast carcinoma risk for women who were physically active before and after menarche (RR = 1.25; 95% CI, 0.98–1.59) compared with women who never participated in a sport (Table 5).

We stratified the data according to baseline BMI, baseline energy intake, and weight gain/loss during adult life. In every BMI category we found a reduction in risk associated with baseline recreational physical activity, although none of these reductions were statistically significant. However, in the overweight category (BMI of 25–30) we found a somewhat stronger association (RR = 0.67; 95% CI, 0.42–1.08, $P = 0.01$) (Table 6) between baseline recreational physical activity and breast carcinoma risk.

According to baseline energy intake, the results also showed nonsignificant reductions in risk associated with baseline recreational physical activity and

TABLE 4
Age-Adjusted and Multivariate RRs of Postmenopausal Breast Carcinoma According to History of Sports Participation, Intensity Scores Regarding History of Sports Participation, and Occupational Physical Activity (the Netherlands Cohort Study, 1986–1993)

	Cases	Person-years	RR[a]	RR[b]	95% CI	*P* value
History of sports participation						
Never participated in sports	478	5202	1.00[c]	1.00[c]		
Ever participated in sports	471	4339	1.17	1.13	0.94–1.37	
No. of hrs of sports per week						
< 1	91	862	1.00[c]	1.00[c]		
1–2	107	962	1.07	0.98	0.65–1.47	
2–3	54	530	0.97	0.88	0.55–1.40	
3–5	66	716	0.84	0.76	0.49–1.19	
> 5	127	1117	1.06	0.87	0.57–1.32	0.14
Sports duration (yrs)						
1–10	231	2140	1.00[c]	1.00[c]		
11–20	97	816	1.06	0.97	0.68–1.38	
21–30	33	360	0.79	0.83	0.50–1.37	
31–40	23	296	0.69	0.66	0.37–1.19	
> 40	42	324	1.20	0.99	0.58–1.67	0.28
Mean MET score per year						
< 4	63	652	1.00	1.00		
4.01–6.00	178	1583	1.09	1.11	0.74–1.66	
> 6.00	187	1690	1.12	1.07	0.71–1.60	0.74
Occupational physical activity						
Longest held job						
Energy expenditure (kJ/min)						
< 8	459	4246	1.00[c]	1.00[c]		
8–12	263	2425	1.00	1.13	0.89–1.44	
> 12	33	433	0.77	0.83	0.51–1.34	0.69
Sitting time per day (hrs)						
6–8	250	2430	1.00[c]	1.00[c]		
2–6	177	1632	1.00	1.19	0.88–1.60	
< 2	328	3045	1.07	1.21	0.94–1.56	0.54
Last held job						
Energy expenditure (kJ/min)						
< 8	475	4373	1.00[c]	1.00[c]		
8–12	256	2444	0.97	1.07	0.84–1.37	
> 12	40	433	0.88	0.98	0.62–1.55	0.73
Sitting time per day (hrs)						
6–8	260	2474	1.00[c]	1.00[c]		
2–6	197	1729	1.04	1.24	0.92–1.65	
< 2	314	3047	1.03	1.10	0.85–1.42	0.68

RR: rate ratio; 95% CI: 95% confidence interval; MET score: the ratio of the associated metabolic rate for the specific activity divided by the resting metabolic rate (intensity score).

[a] Age-adjusted analysis.

[b] Multivariate analysis adjusted for age, age at menarche, age at menopause, benign breast disease, parity, age at first birth, maternal breast carcinoma, breast carcinoma in sister(s), education, height, and baseline alcohol and energy intake.

[c] Reference category.

with borderline significant trends, except for the lowest quintile. Women in the second quintile of energy intake and who were active for > 90 minutes a day showed a decreased breast carcinoma risk (RR = 0.66; 95% CI, 0.34–1.27, $P = 0.05$) compared with women who were active < 30 minutes a day. Even women in the highest quintile of energy intake and who were active for > 90 minutes a day had an RR of 0.85 (95% CI, 0.42–1.71; $P = 0.07$) compared with women who were active < 30 minutes a day.

According to weight gain/loss during adult life, the results also showed a reduction in breast carcinoma risk associated with baseline recreational physical activity. Women who had a weight gain of 10–17 kg during adult life (from age 20 years until baseline) showed an RR of 0.55 (95% CI, 0.29–1.04) with a significant trend ($P = 0.004$). For women who had a weight gain of > 17 kg, a reduction in breast cancer risk still was observed (although not significant), which was associated with baseline recreational phys-

TABLE 5
Multivariate RRs of Postmenopausal Breast Carcinoma According to Sports Participation in Different Time Periods in a Woman's Life (the Netherlands Cohort Study, 1986–1993)

	Cases	Person-years	RR[a]	95% CI	*P* value
Time windows					
Age 20 yrs					
Never participated in sports	478	5205	1.00[b]		
Participated in sports only before age 20 yrs	81	742	1.22	0.87–1.69	
Participated in sports only after age 20 yrs	107	1026	1.03	0.76–1.40	
Participated in sports before and after age 20 yrs	240	2142	1.16	0.92–1.45	0.17
Birth of first child					
Never participated in sports	478	5205	1.00[b]		
Participated in sports only before birth of first child	172	1688	1.18	0.91–1.52	
Participated in sports only after birth of first child	56	589	1.04	0.69–1.55	
Participated in sports before and after birth of first child	109	994	1.22	0.89–1.67	0.09
Age at menarche[c]					
Never participated in sports	478	5202	1.00[b]		
Participated in sports only after menarche	224	2085	1.04	0.83–1.32	
Participated in sports before and after menarche	190	1717	1.25	0.98–1.59	0.03

RR: rate ratio; 95% CI: 95% confidence interval.

[a] Multivariate analysis adjusted for age, age at menarche, age at menopause, benign breast disease, parity, age at first birth, maternal breast carcinoma, breast carcinoma in sister(s), education, height, and baseline alcohol and energy intake.

[b] Reference category.

[c] The category "participated in sports only before menarche" was too small ($n = 14$) to include in the analysis.

ical activity (RR = 0.70; 95% CI, 0.44–1.67, $P = 0.42$). We found no significant tests of interaction between baseline recreational physical activity, baseline BMI, baseline energy intake, and weight gain/loss during adult life.

We also studied the interaction between baseline recreational physical activity, baseline energy intake, and baseline BMI together (Table 7). In the category of obese women (> 30) the number of cases was too small to conduct a multivariate analysis. Therefore, only age-adjusted analyses are shown for this category. The greatest reduction in risk was observed in the second category of BMI (25–30), independent of energy intake. In the subgroup of women who were overweight with a high baseline energy intake, baseline recreational physical activity was found to be related inversely to breast carcinoma risk (RR = 0.35; 95% CI, 0.1–1.23, $P = 0.002$). Even in the lowest BMI category (< 25), a reduction in risk was observed and energy intake was intermediate (RR = 0.59; 95% CI, 0.29–1.19, $P = 0.05$).

DISCUSSION

The results of the current study support the hypothesis that physical activity protects against breast carcinoma in postmenopausal women. Baseline recreational physical activity showed an inverse association with breast carcinoma risk, especially daily walking and biking > 1 hour a day, which demonstrated a protective effect (RR = 0.81).

Women who were ever engaged in sports before baseline did not have appear to have a lower breast carcinoma risk. No relation was found for the duration of the sport activity in years and breast carcinoma risk. A weak inverse relation was found for the number of hours of sports per week. Women who spent > 5 hours per week participating in a sport had a reduction in breast carcinoma risk of 13% (RR = 0.87) compared with women who spent < 1 hour per week participating in a sport. We found no association between occupational physical activity and breast carcinoma risk.

We could not distinguish a specific period in life in which the association between sports activity and breast carcinoma risk was more pronounced; therefore we believe that the age at which women participate in sports is not related to breast carcinoma risk. Furthermore, in the subgroup of women who were overweight (BMI of 25–30), we found a decreased breast carcinoma risk independent of baseline energy intake.

Before discussing the results of the current study in relation with other studies, some remarks concerning the NLCS are relevant. Loss to follow-up is the primary source of potential selection bias in prospective cohort studies. The prospective nature of a cohort study together with completeness of follow-up, as has been achieved in the current study, reduces the po-

TABLE 6
Multivariate RRs of Postmenopausal Breast Carcinoma According to Categories of Baseline Recreational Physical Activity, Stratified by Baseline BMI (kg/m^2, according to WHO/NIH Standardized Categories), Baseline Energy Intake (in Quintiles), and Weight Gain/Loss during Life (in Quartiles) (the Netherlands Cohort Study, 1986–1993)

	Cases	Person-years	RR[a]	95% CI	*P* value
Baseline BMI (kg/m^2)					
Baseline recreational physical activity (min/day)					
Normal (< 25)					
< 30	118	1035	1.00[b]		
30–60	160	1732	0.86	0.62–1.20	
61–90	113	1242	0.88	0.61–1.25	
> 90	97	1212	0.74	0.52–1.08	0.05
Overweight (25–30)					
< 30	97	774	1.00[b]		
30–60	121	1119	0.76	0.51–1.13	
61–90	70	694	0.66	0.41–1.06	
> 90	79	741	0.67	0.42–1.08	0.01
Obese (> 30)					
< 30	30	277	1.00[b]		
30–60	25	225	1.30	0.48–3.52	
61–90	12	186	0.77	0.27–2.22	
> 90	17	153	0.94	0.27–3.32	0.55
Baseline energy intake (quintiles)[c]					
Baseline recreational physical activity (min/day)					
Q1 (low)					
< 30	48	446	1.00[b]		
30–60	53	580	0.81	0.45–1.45	
61–90	43	416	0.97	0.52–1.79	
> 90	32	402	0.77	0.40–1.46	0.53
Q2					
< 30	49	505	1.00[b]		
30–60	62	554	1.17	0.66–2.07	
61–90	32	349	0.95	0.47–1.92	
> 90	31	472	0.66	0.34–1.27	0.05
Q3					
< 30	58	334	1.00[b]		
30–60	70	654	0.64	0.37–1.10	
61–90	51	475	0.60	0.33–1.08	
> 90	45	379	0.67	0.35–1.28	0.06
Q4					
< 30	53	425	1.00[b]		
30–60	60	633	0.72	0.39–1.31	
61–90	40	453	0.63	0.34–1.19	
> 90	32	353	0.70	0.36–1.36	0.08
Q5 (high)					
< 30	38	363	1.00[b]		
30–60	62	662	0.82	0.45–1.51	
61–90	29	435	0.68	0.36–1.30	
> 90	53	505	0.85	0.42–1.71	0.07
Weight gain/loss (in quartiles)					
Baseline recreational physical activity (min/day)					
1 (−35 kg–+5 kg)					
< 30	43	403	1.00[b]		
30–60	62	644	1.07	0.59–1.34	
61–90	42	630	0.73	0.40–1.34	
> 90	36	617	0.72	0.38–1.35	0.05
2 (5–10 kg)					
< 30	39	353	1.00[b]		
30–60	61	684	0.71	0.38–1.34	
61–90	48	406	1.15	0.60–2.18	
> 90	42	399	0.95	0.49–1.87	0.52
3 (10–17 kg)					
< 30	60	558	1.00[b]		
30–60	86	798	0.85	0.52–1.38	
61–90	46	448	0.72	0.39–1.32	
> 90	46	508	0.55	0.29–1.04	0.004
4 (> 17 kg)					
< 30	72	590	1.00[b]		
30–60	65	685	0.72	0.53–1.52	
61–90	46	455	0.63	0.46–1.59	
> 90	51	439	0.70	0.44–1.67	0.42

RR: rate ratio; BMI: body mass index; WHO/NIH: World Health Organization/National Institutes of Health; 95% CI: 95% confidence interval.

[a] Multivariate analysis adjusted for age, age at menarche, age at menopause, benign breast disease, parity, age at first birth, maternal breast carcinoma, breast carcinoma in sister(s), education, height, and baseline alcohol use and energy intake.

[b] Reference category.

[c] Multivariate model without baseline energy intake.

TABLE 7
Multivariate RR of Postmenopausal Breast Carcinoma According to Categories of Baseline Recreational Physical Activity, Stratified by Energy Intake (in Tertiles) and BMI (kg/m^2, According to WHO/NIH Standardized Categories) (the Netherlands Cohort Study, 1986–1993)

		Baseline recreational physical activity				
BMI (kg/m^2)	Energy intake[a] (kcal) (tertiles)	< 30 min/day RR (95% CI)	30–60 min/day RR[b] (95% CI)	60–90 min/day RR[b] (95% CI)	> 90 min/day RR[b] (95% CI)	*P* value
Normal (< 25)	Low	1.00[c]	1.07 (0.50–2.30)	1.25 (0.57–2.78)	0.63 (0.27–1.46)	0.28
	Intermediate	1.00[c]	0.67 (0.37–1.21)	0.73 (0.38–1.40)	0.59 (0.29–1.19)	0.05
	High	1.00[c]	0.86 (0.48–1.54)	0.77 (0.42–1.40)	0.83 (0.45–1.53)	0.36
Overweight (25–30)	Low	1.00[c]	0.83 (0.36–1.91)	1.13 (0.43–3.02)	0.90 (0.36–2.23)	0.97
	Intermediate	1.00[c]	0.78 (0.40–1.54)	0.73 (0.32–1.65)	0.61 (0.27–1.38)	0.25
	High	1.00[c]	0.49 (0.19–1.07)	0.37 (0.14–1.00)	0.35 (0.10–1.23)	0.002
Obese[d] (> 30)	Low	1.00[c]	1.08 (0.67–1.73)	0.83 (0.50–1.39)	0.91 (0.54–1.52)	0.35
	Intermediate	1.00[c]	0.75 (0.42–1.33)	0.49 (0.24–1.01)	0.71 (0.37–1.36)	0.07
	High	1.00[c]	0.88 (0.27–2.89)	0.48 (0.11–2.09)	0.56 (0.11–2.79)	0.18

RR: rate ratio; BMI: body mass index; WHO/NIH: World Health Organization/National Institutes of Health; 95% CI: 95% confidence interval.

[a] Categories of energy intake: low, < 1455 kcal; intermediate, 1455–1789 kcal; and high > 1789 kcal. Body mass index was based on standardized categories according to the World Health Organization/National Institutes of Health.

[b] Multivariate analysis adjusted for age, age at menarche, age at menopause, benign breast disease, parity, age at first birth, maternal breast carcinoma, breast carcinoma in sister(s), education, height and baseline alcohol use.

[c] Reference category.

[d] Only age-adjusted because the numbers of cases in the subgroups were too small.

tential for selection bias to a minimum.[34] Because we considered the most important potential confounding factors reported in the literature and included all factors associated with breast carcinoma risk or the exposure variables in the current study in the multivariate model (e.g., age, reproductive factors, baseline energy, and alcohol intake), we believe that only unmeasured or still unknown other factors may have caused residual confounding.

Measuring physical activity in epidemiologic studies is difficult, and different methods have been used, which may explain in part the inconsistent results across studies.[2] Studies have differed with regard to the following parameters: the period for which physical activity was assessed (i.e., childhood/adolescence, lifetime, etc.), the sources of physical activity (i.e., recreational, occupational, or both), and the various parameters of activity (i.e., frequency, intensity, duration). In the current study the baseline recreational physical activity was measured by several aspects including gardening/doing odd jobs, biking/walking during leisure time, daily walking and biking (taking out the dog, going shopping), and participating in sports/gymnastics. We made use of the history of sports participation as an indicator of physical activity in the past. We were not able to achieve a complete overview of all the elements of past physical activity (e.g., gardening and house keeping activities were not included). Misclassification and recall bias might play a role in determining the exposure status of the participants early in life. Because such misclassification would be unrelated to disease status (nondifferential), it should underestimate any true association between lifetime recreational physical activity and breast carcinoma risk.

Especially for the women in our Dutch cohort (ages 55–69 years) it was not as common to participate in a sport during adolescence and adulthood as it is today. Therefore, many cases and subcohort members had never participated in a sport. Currently, approximately 40% of the persons age > 55 years are engaged in at least 1 sport in the Netherlands.[35] Nearly 35% of the subcohort members did participate in a sport at baseline. Thus, at baseline our cohort was more or less comparable to the general Dutch population with regard to sports activities.

The main aim of the NLCS was to investigate the relation between diet and the risk of cancer, with no specific emphasis on physical activity. An advantage of this large-scale prospective cohort study is the possibility to study interactions between the different indicators of energy balance (physical activity, energy intake, and BMI). As the results of the current study show, no interaction was found between baseline recreational physical activity and BMI, baseline energy intake, and weight gain/loss during adult life, although in the subgroup of women with a high BMI an inverse relation was observed between baseline recreational physical activity and breast carcinoma risk, independent of baseline energy intake. Thus, over-

weight women appear to have a lower breast carcinoma risk if they exercise daily for > 90 minutes compared with heavy women who exercise daily < 30 minutes, regardless of their energy intake. A recent case–control study[36] suggested that frequent episodes of strenuous physical activity during young adulthood may have the greatest benefits for reducing postmenopausal breast carcinoma risk, but only in women who avoid weight gain during adult life. If women gain substantive weight during adulthood, the benefits of frequent and strenuous early life physical activity appear to be lost. In the current study cohort the results showed that women who gained weight (> 17 kg) still had a reduction in breast carcinoma risk associated with baseline recreational physical activity. However, the relation between body size, energy intake, and physical activity requires further research. BMI is only a gross measurement of body composition and does not provide information regarding the percentages of lean and fat masses, nor concerning the distribution of body mass.

For some aspects of past physical (sport) activity (hours of sports per week) the results showed a possible U-shaped relation with breast carcinoma risk. Moderate physical activity may enhance the immune system by elevating the number of natural killer cells whereas exhaustive physical exercise may depress immunologic function.[23] Other authors have stated that the relation between physical exercise and immune function follows a "J"-shaped curve, with the lowest risk observed among women who undertake regular moderate exercise.[37]

Sports participation during specific periods in life was not found to be related to breast carcinoma risk in the current study cohort. Some of the studies that assessed physical activity during adolescence and/or young adulthood observed a reduction in subsequent breast carcinoma risk,[7,14,16] whereas others found no association.[8,15,38]

The results of the current study showed no association between occupational physical activity and breast carcinoma risk. This is in agreement with the study by Coogan et al., which demonstrated that holding a job of medium/heavy activity did not appear to reduce breast carcinoma risk.[39] The assessment of occupational activity was based on job title and the coding system was based on the Dutch situation; however, there may be large variations in physical activity within one job. This variation could not be included in the assessment of occupational physical activity. Women who had held 1 job for a very short period (< 5 years) and a long time previously (e.g. when they were ages 20–25 years) were categorized into physical activity scores according to this job (for the longest as well as the latest job). Their physical activity pattern during the rest of their life perhaps is not in comparison with the period during which they worked.

The current study supports the hypothesis that physical activity is related inversely to breast carcinoma risk in postmenopausal women. However, we could not distinguish a certain period in life at which it was important to be physically active. The frequency, duration, and intensity of sports activities were not found to be related strongly to breast carcinoma risk in the current study cohort. Baseline BMI and energy intake together showed a somewhat stronger reduction in breast carcinoma risk associated with baseline recreational physical activity in women who were overweight (BMI between 25–30), independent of baseline energy intake.

Further research should be concentrated on the assessment of lifetime physical activity to gain insight into different aspects of physical activity and their relation to breast carcinoma risk. Physical activity is one of the few modifiable, protective factors for breast carcinoma and there are many other important health-related reasons to promote regular exercise.

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